REMARKS

Claims 1-16 and 18-48 are pending in this application. Claims 1-10 and 23-48 are canceled. Claims 11, 14-16, and 20 are amended. Upon entry of this amendment, claims 11-16 and 18-22 will be pending in this application.

Claim 11 is amended to clarify that the crosslinked HA composition is a single hydrated particle phase. No new matter is added by way of this amendment (*see*, *e.g.*, ¶ 50).

Claim 14 is amended to clarify that the bioactive agent includes an anesthetic. Claims 15 and 16 are amended for proper antecedent basis. No new matter is added by way of these amendments (*see*, *e.g.*, ¶ 58).

Claim 20 is amended herein to correct a typographical error. Specifically, the phrase "; and" has been deleted from the end of the claim. No new matter is added by way of this amendment.

The Office Action objected to claim 20 and rejected claims 11-16 and 18-22. Each objection and rejection is addressed individually below. The citations to the specification included throughout this amendment correspond to the paragraph numbers of the published application (US 2005/0136122).

I. Interview Summary

Applicants thank Examiner Haghighatian and Examiner Brown for extending the courtesy of an interview on October 5, 2009. During the interview, Andrew Carter, Mary Rose Scozzafava, and Andrew Zoltan discussed the subject matter of the instant claims and the art cited in the § 103 rejection of the Office Action of April 16, 2009, and presented arguments detailing why the cited art does not render the instant claims obvious. In particular, the primary reference cited in the § 103 rejection discloses two-phase gel slurries, while the instant claims, as amended, recite a single hydrated particle phase. The secondary references do not cure this deficiency. Applicants thank Examiners Haghighatian and Brown for noting that the amendment to claim 11, as listed above, obviates the art cited in the Office Action of April 16, 2009.

II. Objection to Claim 20

The Office Action objected to claim 20 because "Line 4 of claim 20 has '; and' at the end of the claim."

Applicants respectfully submit that the recitation of "; and" in the Amendment in Response to Non-Final Office Action dated September 10, 2008 was a typographical error. This error has been corrected by the present amendment.

Accordingly, Applicants respectfully submit that this objection has overcome, and that it be reconsidered and withdrawn.

III. Rejections Under 35 U.S.C. § 103(a)

The Office Action rejected all claims under 35 U.S.C. § 103(a) as obvious in light of U.S. Patent No. 5,143,724 ("Leshchiner"), Japan Patent No. 2000230001A ("Fujita"), U.S. Patent No. 5,942,241 ("Chasin"), and U.S. Patent No. 7,196,180 ("Aeschlimann"). Applicants disagree with this rejection.

Amended independent claim 11 is listed above. Notably, claim 11 is amended to clarify that the crosslinked HA composition is a single hydrated particle phase. Claims 12-16 and 18-22 depend directly or indirectly from claim 11 and thus include all the limitations of claim 11.

The Supreme Court recently ruled that in an obviousness inquiry:

> [o]ften, it will be necessary … to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate this review, this analysis should be made explicit.

KSR Int'l Co. v. Teleflex, Inc., 127 S. Ct. 1727, 1740-41 (2007). The Supreme Court also stated that "when the prior art teaches away from combining certain known elements, discovery of a successful

means of combining them is more likely to be nonobvious." *Id.* at 1740 (citing *United States v. Adams*, 383 U.S. 39, 51-52 (1966)). Applicants maintain that the cited references does not establish a *prima facie* case of obviousness under this standard.

The Office Action states that "Leshchiner et al. teach the application of biocompatible viscoelastic gel slurries … for soft tissue augmentation wherein the basic properties of the mixed gel slurries include: … injection through a small diameter needle …" (Office Action at pages 4-5, emphasis in original).

Leshchiner discloses "two-phase gel slurries in which the first phase comprises swollen polymeric gel particles uniformly distributed in the second phase which is, preferably, a viscoelastic solution of a polymer" (Leshchiner at col. 2, lines 61-65). Either or both phases may be hyaluronic acid (Leshchiner at col. 2, line 66 to col. 3, line 4; col. 4, lines 40-44).

Leshchiner does not teach or suggest a method of tissue augmentation using a hyaluronic acid composition that is a single hydrated particle phase. In fact, Leshchiner teaches away from the use of crosslinked HA gel particles in a single hydrated particle phase, as Leshchiner touts the advantages of a two-phase composition (*see, e.g.*, col. 2, lines 59-65; col. 8, lines 1-63). Leshchiner also does not disclose or suggest specific particle sizes as required by claims 11-16 and 18-22

Accordingly, Leshchiner does not render claims 11-16 and 18-22 obvious.

The Office Action therefore cites Fujita, stating that Fujita teaches HA gel particles with "an average particle size of 10 mm or smaller (preferably 10-5000 micrometers, see [0019]) and used for injection" (Office Action at page 6, emphasis in original). The Office Action also states that the Fujita compositions have a multimodal size distribution (*id.*).

Fujita does not cure the deficiencies of Leshchiner. Fujita teaches a gel slurry (*see* Fujita at abstract and at ¶¶ 7-8), not gel particles in a single hydrated particle phase. Fujita also teaches that combining hyaluronic acid gel particles with a hyaluronic acid gel will provide an "***enhancement of an effect*** by the composition formula" (Fujita at ¶ 29, emphasis added). Thus Fujita teaches that a

two-phase composition is superior to a single hydrated particle phase, and therefore teaches away from the instant claims.

Furthermore, the Office Action admits that Fujita teaches a "mean particle diameter being 10 mm or less" (Fujita at ¶ 7). This mean diameter is beyond the scope of the instant claims, which recite "an average particle diameter distribution selected from the group consisting of a hydrated particle average diameter between about 20 μm and about 1000 μm, and a dehydrated particle average diameter between about 10 μm and about 500 μm." Fujita also teaches the use of HA that is crosslinked without using a chemical crosslinking agent (Fujita at ¶ 11). Thus Fujita teaches away from the crosslinked HA recited in the instant claims.

Fujita, alone or in combination with Leshchiner, does not teach or suggest to one of ordinary skill in the art how to achieve a single hydrated particle phase. Accordingly, the combination of Fujita and Leshchiner do not render the instant claims obvious.

Chasin does not address or cure the deficiencies of Fujita and Leshchiner. Chasin teaches "pharmaceutically acceptable augmenting agent or agents in conjunction with a local anesthetic in controlled release form that significantly increases the time period of local anesthesia when administered at a site in a patient" (Chasin at col. 5, lines 31-27). The "augmenting agents" used in Chasin's invention "are compositions or compounds that prolong the duration of local anesthesia and/or enhance the effectiveness of local anesthetic agents when delivered to the site of local anesthetic administration before, simultaneously with or after the local anesthetic is administered" (Chasin at col. 6, lines 59-64). Chasin does not disclose the use of a single hydrated particle phase of crosslinked HA gel particles in a method for tissue augmentation.

Aeschlimann fails to cure the deficiencies of Leshchiner, Fujita, and Chasin. Aeschlimann discloses a "method for chemical crosslinking of high molecular weight hyaluronic acid under physiological conditions" (Aeschlimann at col. 5, lines 12-14). Aeschlimann is silent with regard to the use of a single hydrated particle phase of crosslinked HA gel particles. Therefore, Aeschlimann provides no teaching or suggestion for one of ordinary skill in the art to create the subject matter of the instant claims.

Leshchiner, Fujita, Chasin, and Aeschlimann, alone or in combination, fail to render the instant claims obvious. In particular, none of these references teach or suggest how to make a single hydrated particle phase of crosslinked HA gel particles for use in a method of tissue augmentation where the HA gel particles are injected into a patient.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a) of claims 11-16 and 18-22.

CONCLUSION

In view of the above amendments and arguments, Applicants submit that the objection and rejections in the Office Action of April 16, 2009 have been overcome and that the pending claims are in condition for allowance.

A request for a three-month extension of time is submitted with this response. Please charge the required fee to our Deposit Account No. 08-0219, under Order No. 0103343.00128US1, from which the undersigned is authorized to draw. Please charge any other payments due or credit any overpayments owed to our Deposit Account No. 08-0219, under Order No. 0103343.00128US1, from which the undersigned is authorized to draw.

Respectfully submitted,

Dated: October 8, 2009

/Andrew Zoltan/
Andrew Zoltan
Registration No.: 64,929
Attorney for Applicant(s)

Wilmer Cutler Pickering Hale and Dorr LLP
399 Park Avenue
New York, NY 10022
(212) 230-8800 (telephone)
(212) 230-8888 (facsimile)